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Welcome to STN International
                 Web Page URLs for STN Seminar Schedule - N. America
NEWS
                 IMSworld Pharmaceutical Company Directory name change
NEWS
        Sep 17
     2
                 to PHARMASEARCH
                 Korean abstracts now included in Derwent World Patents
NEWS
        Oct 09
                Number of Derwent World Patents Index updates increased
NEWS
        Oct 09
NEWS 5 Oct 15
                Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS 6 Oct 22
                Over 1 million reactions added to CASREACT
NEWS 7
        Oct 22
                DGENE GETSIM has been improved
NEWS 8 Oct 29 AAASD no longer available
NEWS 9
        Nov 19 New Search Capabilities USPATFULL and USPAT2
NEWS 10 Nov 19
                TOXCENTER(SM) - new toxicology file now available on STN
                COPPERLIT now available on STN
NEWS 11 Nov 29
NEWS 12 Nov 29 DWPI revisions to NTIS and US Provisional Numbers
                Files VETU and VETB to have open access
NEWS 13 Nov 30
NEWS 14 Dec 10
                WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS 15 Dec 10
                DGENE BLAST Homology Search
NEWS 16 Dec 17
                WELDASEARCH now available on STN
NEWS 17 Dec 17
                STANDARDS now available on STN
NEWS 18 Dec 17 New fields for DPCI
NEWS 19 Dec 19 CAS Roles modified
NEWS 20 Dec 19
                1907-1946 data and page images added to CA and CAplus
NEWS 21
        Jan 25
                BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 22
                Searching with the P indicator for Preparations
        Jan 25
NEWS 23
                FSTA has been reloaded and moves to weekly updates
        Jan 29
                DKILIT now produced by FIZ Karlsruhe and has a new update
NEWS 24
        Feb 01
                 frequency
NEWS 25
        Feb 19
                Access via Tymnet and SprintNet Eliminated Effective 3/31/02
                Gene Names now available in BIOSIS
NEWS 26 Mar 08
             February 1 CURRENT WINDOWS VERSION IS V6.0d,
NEWS EXPRESS
              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS
              STN Operating Hours Plus Help Desk Availability
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              Welcome Banner and News Items
NEWS PHONE
             Direct Dial and Telecommunication Network Access to STN
NEWS WWW
             CAS World Wide Web Site (general information)
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FILE 'HOME' ENTERED AT 16:10:02 ON 13 MAR 2002

=> file caplus, uspatfull, wpids, toxlit, toxline, drugu, medline, biosis 'TOXLINE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue

thalidomide precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and NSAIDs can inhibit angiogenesis-dependent

diseases either alone or in combination with thalidomide and related compds. Importantly, these compds. can be administered orally.

L25 ANSWER 13 OF 15 USPATFULL

AN 1998:14828 USPATFULL

TI Anti-angiogenic compositions and methods of use

IN Hunter, William L., Vancouver, Canada Machan, Lindsay S., Vancouver, Canada Arsenault, A. Larry, Paris, Canada

Angiogenesis Technologies, Inc., Vancouver, Canada (non-U.S.

corporation)

PI US 5716981 19980210

AI US 1995-478203 19950607 (8)

RLI Division of Ser. No. US 1995-417160, filed on 3 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1993-94536, filed on 19 Jul 1993, now abandoned

PRAI WO 1994-CA373 19940719

DT Utility FS Granted

PA

EXNAM Primary Examiner: Kumar, Shailendra

LREP Seed and Berry LLP
CLMN Number of Claims: 18
ECL Exemplary Claim: 1

DRWN 130 Drawing Figure(s); 75 Drawing Page(s)

LN.CNT 5084

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides compositions comprising an anti-angiogenic factor, and a polymeric carrier. Representative examples of anti-angiogenic factors include Anti-Invasive Factor, Retinoic acids and derivatives thereof, and paclitaxel. Also provided are methods for embolizing blood vessels, and eliminating biliary, urethral, esophageal, and tracheal/bronchial obstructions.

L25 ANSWER 14 OF 15 TOXLIT

AN 1998:81623 TOXLIT

DN CA-129-012742P

TI Methods and compositions using thalidomide or other angiogenesisinhibitory compound and anti-inflammatory agent for inhibition of angiogenesis.

AU D'Amato RJ

SO (1998). PCT Int. Appl. PATENT NO. 9819649 05/14/1998 (Children's Medical Center).

CODEN: PIXXD2.

CY UNITED STATES

DT Patent

FS CA

LA English

OS CA 129:12742

EM 199807

AB A group of compds. that effectively inhibit angiogenesis is provided. More specifically, thalidomide and various related compds.,e.g. thalidomide precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit angiogenesis and to treat disease states resulting from angiogenesis. Addnl., antiinflammatory drugs, such as steroids and NSAIDs can inhibit angiogenesis-dependent diseases either alone or in combination with thalidomide and related compds. Importantly, these compds. can be administered orally.

L25 ANSWER 15 OF 15 MEDLINE

DZS ANSWER 15 OF 15 MEDILI

AN 92249916 MEDLINE

```
DN 92249916 PubMed ID: 1577394
```

- TI Mechanisms of gastric and duodenal damage and protection.
- AU Hudson N; Hawthorne A B; Cole A T; Jones P D; Hawkey C J
- CS Department of Therapeutics, University Hospital, Nottingham, U.K.
- SO HEPATO-GASTROENTEROLOGY, (1992 Feb) 39 Suppl 1 31-6. Ref: 47 Journal code: GA7; 8007849. ISSN: 0172-6390.
- CY GERMANY: Germany, Federal Republic of
- DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

- LA English
- FS Priority Journals
- EM 199206
- ED Entered STN: 19920619 Last Updated on STN: 19920619

Entered Medline: 19920610

By binding to the cyclooxygenase enzyme, non-steroidal, anti-inflammatory AB drugs (NSAIDs) inhibit synthesis of prostanoids characteristic of the cell under consideration. For the gastric mucosa, the main products are prostaglandin (PG) E2 or PGI2; for platelets the main product is thromboxane. Aspirin irreversibly acetylates the cyclooxygenase enzyme. Consequently, it has more prolonged effects, particularly in cells like platelets, which are not rapidly turned over. Prostaglandin-dependent protective actions in the stomach and duodenum which are inhibited by NSAIDs include mucous and bicarbonate secretion, surface epithelial cell hydrophobicity and mucosal blood flow. Prostaglandins are also protective of the microvasculature and can increase the flux of water from serosa to mucosa, with possible dilution of injurious substances. Abrogation of these properties renders the mucosa more vulnerable to injury. In addition, salicylates have topical irritant properties. A number of repair mechanisms, including epithelial cell division and possibly angiogenesis, are prostaglandin dependent. As a consequence of these actions, acute damage and ulcers develop more easily and ulcers heal more slowly when individuals take NSAIDs. In some cases the anti-hemostatic effects of NSAIDs may be partly instrumental, and data in model systems have shown that aspirin and possibly piroxicam can enhance intragastric bleeding separately from their effects of mucosal injury. Smoking, which predisposes to peptic ulceration, also appears to reduce mucosal prostaglandin synthesis. Other predisposing factors such as age, sex and the ulcer diathesis have little effect. Some have found Helicobacter pylori to enhance leukotriene synthesis. We have shown that NSAIDs are also associated with increased leukotriene B4 as well as reduced prostaglandin synthesis in patients taking NSAIDs long term.

```
ANSWER 11 OF 15 USPATFULL
L25
      1999:37140 USPATFULL
AN
ТT
      Anti-angiogenic compositions and methods of use
      Hunter, William L., Vancouver, Canada
TN
      Machan, Lindsay S., Vancouver, Canada
      Arsenault, A. Larry, Paris, Canada
      Angiotech Pharmaceuticals Inc., Vancouver, Canada (non-U.S. corporation)
PA
PΙ
      US 5886026
                              19990323
ΑI
      US 1995-472413
                              19950607 (8)
      Division of Ser. No. US 1995-417160, filed on 3 Apr 1995, now abandoned
RLT
      which is a continuation-in-part of Ser. No. US 1993-94536, filed on 19
      Jul 1993, now abandoned
                         19940719
PRAI
      WO 1994-CA373
DT
      Utility
FS
      Granted
EXNAM Primary Examiner: Kumar, Shailendra
      Seed and Berry LLP
LREP
CLMN
      Number of Claims: 6
ECL
      Exemplary Claim: 1
DRWN
      130 Drawing Figure(s); 75 Drawing Page(s)
LN.CNT 4997
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      The present invention provides compositions comprising an
AB
      anti-angiogenic factor, and a polymeric carrier. Representative examples
      of anti-angiogenic factors include Anti-Invasive Factor, Retinoic acids
      and derivatives thereof, and paclitaxel. Also provided are methods for
      embolizing blood vessels, and eliminating biliary, urethral, esophageal,
       and tracheal/bronchial obstructions.
L25 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS
                                                      DUPLICATE 2
AN
    1998:341491 CAPLUS
DN
    129:12742
    Methods and compositions using thalidomide or other angiogenesis-
TT
     inhibitory compound and anti-inflammatory agent for inhibition of
    angiogenesis
    D'Amato, Robert J.
IN
PΑ
    Children's Medical Center, USA
SO
    PCT Int. Appl., 63 pp.
    CODEN: PIXXD2
DT
    Patent
T.A
    English
FAN.CNT 1
                    KIND DATE
    PATENT NO.
                                         APPLICATION NO. DATE
     -----
                                          _____
PТ
    WO 9819649
                     A2
                           19980514
                                         WO 1997-US20116 19971104
    WO 9819649
                     A3
                           19980625
        W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,
            EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT,
            RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN,
            YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
            GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
            GN, ML, MR, NE, SN, TD, TG
    AU 9851973
                                          AU 1998-51973
                    A1
                           19980529
                                                           19971104
                                         EP 1997-946884
    EP 963200
                           19991215
                                                           19971104
                      A2
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
PRAI US 1996-28708
                           19961105
    US 1997-963058
                           19971103
    WO 1997-US20116
                           19971104
os
    MARPAT 129:12742
AB
    A group of compds. that effectively inhibit angiogenesis is provided.
    More specifically, thalidomide and various related compds.,e.g.
```

```
ANSWER 9 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
L25
AN
     2000:149600 BIOSIS
DN
     PREV200000149600
ΤI
     Interleukin 12 and indomethacin exert a synergistic, angiogenesis
     -dependent antitumor activity in mice.
     Golab, Jakub (1); Kozar, Katarzyna; Kaminski, Rafal; Czajka, Anna;
ΑU
     Marczak, Maria; Switaj, Tomasz; Giermasz, Adam; Stoklosa, Tomasz; Lasek,
     Witold; Zagozdzon, Radoslaw; Mucha, Krzysztof; Jakobisiak, Marek
CS
     (1) Department of Immunology, Institute of Biostructure, Medical
     University of Warsaw, ul. Chalubinskiego 5, 02-004, Warsaw Poland
SO
     Life Sciences., (Feb. 18, 2000) Vol. 66, No. 13, pp. 1223-1230.
     ISSN: 0024-3205.
DT
     Article
LA
     English
SL
     English
AB
     Nonsteroidal anti-inflammatory drugs have been shown to reduce the
     incidence and mortality from colorectal cancer. It has recently been
     demonstrated that these drugs are capable of suppressing the production of
     pro-angiogenic factors from tumor cells. The mechanisms of antitumor
     action of interleukin 12 include the enforced secretion of anti-angiogenic
     factors and stimulation of antitumor immunity. Therefore, we hypothesized
     that the combination of a model nonsteroidal anti-inflammatory drug -
     indomethacin and interleukin 12 would result in enhanced
     angiogenesis-dependent antitumor effects against a
     colon-26 carcinoma cells transplanted into syngeneic mice. As expected the
     combined administration of both agents simultaneously resulted in a
     strengthened antitumor activity that was manifested as a retardation of
     tumor growth and prolongation of mouse survival. Importantly some mice
     were completely cured after the combined treatment. As administration of
     interleukin 12 and indomethacin resulted in enhanced inhibition of
     angiogenesis it seems possible that prevention of new blood vessel
     formation is one of the mechanisms responsible for the observed antitumor
     effects.
L25
    ANSWER 10 OF 15 USPATFULL
AN
       1999:155724 USPATFULL
TI
       Anti-angiogenic Compositions and methods for the treatment of arthritis
IN
       Hunter, William L., Vancouver, Canada
       Machan, Lindsay S., Vancouver, Canada
       Arsenault, A. Larry, Paris, Canada
PA
       Angiogenesis Technologies, Inc., Vancouver, Canada (non-U.S.
       corporation)
PΙ
       US 5994341
                               19991130
ΑI
      US 1995-478914
                               19950607 (8)
RLI
      Division of Ser. No. US 1995-417160, filed on 3 Apr 1995, now abandoned
       which is a continuation-in-part of Ser. No. US 1993-94536, filed on 19
      Jul 1993, now abandoned
PRAI
      WO 1994-CA373
                           19940719
DT
      Utility
FS
      Granted
EXNAM Primary Examiner: Kumar, Shailendra
LREP
      Seed & Berry LLP
CLMN
      Number of Claims: 8
ECL
      Exemplary Claim: 1
       129 Drawing Figure(s); 75 Drawing Page(s)
LN.CNT 5044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides compositions comprising an
       anti-angiogenic factor, and a polymeric carrier. Representative examples
       of anti-angiogenic factors include Anti-Invasive Factor, Retinoic acids
       and derivatives thereof, and paclitaxel. Also provided are methods for
       embolizing blood vessels, and eliminating biliary, urethral, esophageal,
       and tracheal/bronchial obstructions.
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Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
 PΑ
                    B1 20010612
 PΙ
       US 6245759
                                20000307 (9)
ΑI
       US 2000-519780
                          19990311 (60)
 PRAI
       US 1999-123902
DT
       Utility
FS
       GRANTED
EXNAM Primary Examiner: Ford, John M.; Assistant Examiner: Liu, Hong
       Garcia-Rivas, J. Antonio, Daniel, Mark R.
       Number of Claims: 3
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1300
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to pyrazolo-pyrimidinyl compounds which
       inhibit, regulate and/or modulate tyrosine kinase signal transduction,
       compositions which contain these compounds, and methods of using them to
       treat tyrosine kinase-dependent diseases and conditions, such as
       angiogenesis, cancer, tumor growth, atherosclerosis, age related macular
       degeneration, diabetic retinopathy, inflammatory diseases, and the like
       in mammals.
L25 ANSWER 8 OF 15
                                                         DUPLICATE 1
                        MEDLINE
                    MEDLINE
AN
     2001538698
     21469522 PubMed ID: 11586092
DN
 ΤI
     Targeting angiogenic processes by combination rofecoxib and ionizing
     radiation.
     Dicker A P; Williams T L; Grant D S
· AII
     Department of Radiation Oncology, Kimmel Cancer Center, Jefferson Medical
CS
     College, Thomas Jefferson University, Philadelphia, Pennsylvania
     19107-5097, USA.
NC
     P30 CA 56036-03 (NCI)
     AMERICAN JOURNAL OF CLINICAL ONCOLOGY, (2001 Oct) 24 (5) 438-42.
SO
     Journal code: 3EZ; 8207754. ISSN: 0277-3732.
CY
     United States
DT
     Journal; Article; (JOURNAL ARTICLE)
LΑ
     English
FS
     Priority Journals
EM
     200111
ED
     Entered STN: 20011008
     Last Updated on STN: 20011105
     Entered Medline: 20011101
AB
     Tumor growth and angiogenesis are interdependent. Cyclooxygenase (COX)
     catalyzes the synthesis of prostaglandins from arachidonic acid.
     Nonsteroidal antiinflammatory drugs (NSAIDs)
     inhibit COX-mediated synthesis of prostaglandins. COX-1 is constitutively
     expressed in a wide range of tissues, whereas COX-2 is cytokine inducible.
     Enhanced COX-2 expression has been attributed a key role in the
     development of inflammation and related processes observed in
     pathologically altered disease states. Two specific COX-2 inhibitors,
     namely rofecoxib (Vioxx) and celecoxib (Celebrex), both oral agents and
     U.S. Food and Drug Administration approved, have been shown preclinically
     and clinically to have efficacy comparable to that of NSAIDs for
     relief of pain and inflammation in osteoarthritis, with decreased risk of
     gastrointestinal damage. Little is known about how angiogenesis is
     affected by the combination of rofecoxib and radiation. We have evaluated
     the combination of rofecoxib, at various concentrations, and radiation on
     cytokine-induced angiogenesis in vitro. We have found that rofecoxib
     inhibited endothelial cell proliferation, migration, and tube formation
     (differentiation) at clinically relevant doses. In combination with
     radiation, inhibition of endothelial cell function further increased
     twofold. The combination of rofecoxib and radiation suggests a
     complementary strategy with clinical ramifications to target
     angiogenesis-dependent malignancies.
```

```
Fraley, Mark E., North Wales, PA, United States
IN
       Arrington, Kenneth L., Elkins Park, PA, United States
       Bilodeau, Mark T., Lansdale, PA, United States
       Hartman, George D., Lansdale, PA, United States
       Hoffman, William F., Lansdale, PA, United States
       Kim, Yuntae, Harleysville, PA, United States
       Hungate, Randall W., Newbury Park, CA, United States
PA
       Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
ΡI
       US 6306874
                          В1
                               20011023
ΑI
       US 2000-690598
                               20001017 (9)
PRAI
       US 1999-160356
                           19991019 (60)
DT
       Utility
FS
       GRANTED
       Primary Examiner: Shah, Mukund J.; Assistant Examiner: Truong, Tamthom
EXNAM
LREP
       Garcia-Rivas, J. Antonio, Daniel, Mark R.
       Number of Claims: 36
CLMN
ECL
       Exemplary Claim: 1
       No Drawings
DRWN
LN.CNT 3068
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to compounds which inhibit, regulate
       and/or modulate tyrosine kinase signal transduction, compositions which
       contain these compounds, and methods of using them to treat tyrosine
       kinase-dependent diseases and conditions, such as angiogenesis, cancer,
       tumor growth, atherosclerosis, age related macular degeneration,
       diabetic retinopathy, inflammatory diseases, and the like in mammals.
    ANSWER 6 OF 15 USPATFULL
L25
AN
       2001:168122 USPATFULL
ΤI
       Therapeutic agents
       Doyle, Kevin, Nottingham, United Kingdom
IN
       Rafferty, Paul, Westborough, MA, United States
       Steele, Robert, Nottingham, United Kingdom
       Turner, Allyson, Nottingham, United Kingdom
       Wilkins, David, Nottingham, United Kingdom
       Arnold, Lee, Westborough, MA, United States
       BASF Aktiengesellschaft, Germany, Federal Republic of (non-U.S.
PA
       corporation)
       US 6297238
PΙ
                               20011002
                          B1
ΑI
       US 2000-689943
                               20001012 (9)
       Continuation-in-part of Ser. No. US 2000-541336, filed on 3 Apr 2000
RLI
PRAI
       US 1999-127963 19990406 (60)
DT
       Utility
FS
       GRANTED
EXNAM
      Primary Examiner: Ramseur, Robert W.
LREP
       Hamilton, Brook, Smith & Reynolds, PC
CLMN
       Number of Claims: 42
ECL
       Exemplary Claim: 1
       No Drawings
LN.CNT 3014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention realtes to compounds formula I ##STR1##
AB
       and pharmaceutically acceptable salts thereof, which are inhibitors of
       protein kinase activity, pharmaceutical compositions thereof and
       provesses for their preparation.
L25 ANSWER 7 OF 15 USPATFULL
AN
       2001:86461 USPATFULL
ΤI
       Tyrosine kinase inhibitors
       Bilodeau, Mark T., Lansdale, PA, United States
IN
       Fraley, Mark E., North Wales, PA, United States
```

Hungate, Randall W., Lansdale, PA, United States

```
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to novel human RIP polypeptides and
       isolated nucleic acids containing the coding regions of the genes
       encoding such polypeptides. Also provided are vectors, host cells,
       antibodies, and recombinant methods for producing human RIP
       polypeptides. The invention further relates to diagnostic and
       therapeutic methods useful for diagnosing and treating disorders related
       to these novel human RIP polypeptides.
L25 ANSWER 3 OF 15 USPATFULL
       2001:212454 USPATFULL
AN
TI
       Tyrosine kinase inhibitors
TN
       Fraley, Mark E., North Wales, PA, United States
       Hartman, George D., Lansdale, PA, United States
       Hungate, Randall W., Newbury Park, CA, United States
PΤ
       US 2001044451
                         A1
                               20011122
ΑI
       US 2001-788718
                          A1
                               20010220 (9)
                           20000225 (60)
PRAI
       US 2000-185023
DT
       Utility
FS
       APPLICATION
       MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
LREP
CLMN
       Number of Claims: 32
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 2114
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to compounds which inhibit, regulate
       and/or modulate tyrosine kinase signal transduction, compositions which
       contain these compounds, and methods of using them to treat tyrosine
       kinase-dependent diseases and conditions, such as angiogenesis, cancer,
       tumor growth, atherosclerosis, age related macular degeneration,
       diabetic retinopathy, inflammatory diseases, and the like in mammals.
L25 ANSWER 4 OF 15 USPATFULL
AN
       2001:197035 USPATFULL
TI
       Tyrosine kinase inhibitors
       Fraley, Mark E., North Wales, PA, United States
IN
       Hartman, George D., Lansdale, PA, United States
       Hartman, Randall W., Newbury Park, CA, United States
PA
       Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PΙ
       US 6313138
                               20011106
                          В1
       US 2001047007
                          Α1
                               20011129
AΤ
       US 2001-788720
                               20010220 (9)
PRAI
       US 2000-185024
                          20000225 (60)
       Utility
DT
FS
       GRANTED
EXNAM Primary Examiner: Dentz, Bernard
       Garcia-Rivas, J. Antonio, Daniel, Mark R.
LREP
       Number of Claims: 32
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 2167
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to compounds which inhibit, regulate
AB
       and/or modulate tyrosine kinase signal transduction, compositions which
       contain these compounds, and methods of using them to treat tyrosine
       kinase-dependent diseases and conditions, such as angiogenesis, cancer,
       tumor growth, atherosclerosis, age related macular degeneration,
       diabetic retinopathy, inflammatory diseases, and the like in mammals.
L25 ANSWER 5 OF 15 USPATFULL
AN
       2001:185309 USPATFULL
```

LN.CNT 11257

ΤI

Tyrosine kinase inhibitors

```
281 S L16 AND L7
L21
L22
             60 S L16 AND L8
=> s angiogenesis(4a)dependent
          1595 ANGIOGENESIS (4A) DEPENDENT
=> s 123 and 13
L24
            17 L23 AND L3
=> dup remove 124
PROCESSING COMPLETED FOR L24
L25
             15 DUP REMOVE L24 (2 DUPLICATES REMOVED)
=> d 125 1-15 bib, ab
     ANSWER 1 OF 15 USPATFULL
L25
ΑN
       2002:47999 USPATFULL
ΤI
       Compositions of non-ionic block copolymers to treat autoimmune,
       proliferative, and inflammatory diseases and methods of use thereof
IN
       Kabanov, Alexander V., omaha, NE, UNITED STATES
       Lemieux, Pierre, Ste-Therese, CANADA
       Guerin, Nadia, Longueil, CANADA
       Alakhov, Valery, Montreal, CANADA
PΙ
       US 2002028190
                               20020307
                          Α1
AΙ
       US 2001-852533
                          A1
                               20010510 (9)
PRAI
       US 2000-203549
                           20000512 (60)
DT
       Utility
FS
       APPLICATION
       MATHEWS, COLLINS, SHEPHERD & GOULD, P.A., 100 THANET CIRCLE; SUITE 306,
LREP
       PRINCETON, NJ, 08540-3674
CLMN
       Number of Claims: 17
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1339
       Compositions comprising non-ionic block copolymers are useful for the
AB
       treatment of autoimmune, inflammatory and proliferative diseases and for
       reducing graft/implantation rejection. The present invention also
       relates to methods of treating animals having various autoimmune,
       inflammatory and proliferative diseases. The present invention also
       relates to methods of reducing inflammation in an animal comprising
       administering the compositions of the invention. Also, the present
       invention relates to methods of reducing autoimmune responses and to
       methods of reducing graft/implantation rejection comprising
       administering the compositions of the inventions. A typical embodiment
       is a mixture of Pluronics
L25 ANSWER 2 OF 15 USPATFULL
AN
       2002:8489 USPATFULL
       Retinoid receptor interacting polynucleotides, polypeptides, and
TΙ
       antibodies
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
IN
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002004489
                          A1
                               20020110
       US 2001-788600
AΙ
                          A1
                               20010221 (9)
RLI
       Continuation-in-part of Ser. No. WO 2000-US22351, filed on 15 Aug 2000,
       UNKNOWN
PRAI ·
      US 1999-148757
                           19990816 (60)
       US 2000-189026
                           20000314 (60)
DT
       Utility
FS
       APPLICATION
LREP
       HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN
       Number of Claims: 22
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
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or CR5R6, CR13R14 = 3-7C satd. ring; or CR13R14 = CO or CS; R7 = H or R8; R8 = phenyl or benzyl (both opt. monosubstd. by halo, alkyl, alkoxy, alkylthio, CN or CF3), alkyl or cycloalkyl; R9, R10 = H, alkyl or cycloalkyl; or R9+R10 = O or S; alkyl, alkoxy have 1-10C unless specified otherwise; cycloalkyl has 3-10C.

Also claimed are the tautomers of furanone cpds. of formula (Ia). The tautomers have formula (IIa) or (IIb).

USE - (I) are used to treat inflammation, and cyclooxygenase (COX) -mediated diseases which can be treated by cpds. that selectively inhibit COX-2 rather than COX-1 (claimed). (I) are used to relieve pain, fever and inflammation of a variety of conditions including rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns, injuries, and following surgical and dental procedures. They may also inhibit cellular neoplastic transformations and metastatic tumour growth and can be used to treat cancer. (I) are also used to treat or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour angiogenesis. (I) inhibit prestanoid-induced smooth muscle contraction by preventing the synthesis of contractile prestanoids and may be used to treat dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are used to treat Alzheimer's disease and to prevent bone loss (osteoporosis).

Admin. is oral, topical, parenteral, by inhalation spray or rectal. Dosage is 0.01-140 mg/kg/day.

ADVANTAGE - (I) is an alternative to a conventional NSAID partic. where NSAID's are contraindicated such as in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal (GI) lesions, GI bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease, or prior to surgery or while taking anticoagulants.

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L18 L19

L20

(FILE 'HOME' ENTERED AT 16:10:02 ON 13 MAR 2002)

FILE 'CAPLUS, USPATFULL, WPIDS, TOXLIT, DRUGU, MEDLINE, BIOSIS' ENTERED AT 16:11:11 ON 13 MAR 2002

```
L1
          32162 S NSAID OR NSAID##
L2
          14637 S NONSTEROIDAL (4A) ANTIINFLAMMATOR######
L3
          41818 S L1 OR L2
L4
        1156548 S CANCER##
         39399 S ULCERATIVE COLITIS
L5
         26917 S SYPHILIS
L6
L7
         243552 S ARTHRITIS
        101544 S LUPUS
L8
L9
           3109 S L1 AND L4
L10
            586 S L1 AND L5
           7531 S L1 AND L7
L11
            751 S L1 AND L8
L12
L13
          61491 S ANGIOGENESIS
              0 S NEOVASCULAR GENERAT####
L14
              0 S NEOVASCULARGENERAT####
L15
           716 S L13 AND L3
L16
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305 S L4 AND L16

619 S L13 AND L5

91 S L16 AND L5

3 S L16 AND L6

or alkyl; R3, R11, R12 = phenyl, benzyl, heteroaryl, heteroarylmethyl (all opt. substd. by 1-2 R'), H, alkyl, CH2OR7, CN, CH2CN, 1-6C fluoroalkyl, F or CON(R7)2; or CR11R12 = CO or 3-7C satd. monocyclic ring; R4 = alkoxy, fluoroalkoxy, alkylthio, OH, OCOR7, SH, SCOR7, OCO2R8, SCO2R8, OCON(R7)2, SCON(R7)2, cycloalkyloxy or cycloalkylthio; R5, R6, R13, R14 = H or alkyl; or CR5R6, CR13R14 = 3-7C satd. ring; or CR13R14 = CO or CS; R7 = H or R8; R8 = phenyl or benzyl (both opt. monosubstd. by halo, alkyl, alkoxy, alkylthio, CN or CF3), alkyl or cycloalkyl; R9, R10 = H, alkyl or cycloalkyl; or R9+R10 = O or S; alkyl, alkoxy have 1-10C unless specified otherwise; cycloalkyl has 3-10C.

Also claimed are the tautomers of furanone cpds. of formula (Ia). The tautomers have formula (IIa) or (IIb).

USE - (I) are used to treat inflammation, and cyclooxygenase (COX)-mediated diseases which can be treated by cpds. that selectively inhibit COX-2 rather than COX-1 (claimed). (I) are used to relieve pain, fever and inflammation of a variety of conditions including rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), qout and ankylosing spondylitis, bursitis, burns, injuries, and following surgical and dental procedures. They may also inhibit cellular neoplastic transformations and metastatic tumour growth and can be used to treat cancer. (I) are also used to treat or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour angiogenesis. (I) inhibit prestanoid-induced smooth muscle contraction by preventing the synthesis of contractile prestanoids and may be used to treat dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are used to treat Alzheimer's disease and to prevent bone loss (osteoporosis).

Admin. is oral, topical, parenteral, by inhalation spray or rectal. Dosage is 0.01-140 mg/kg/day.

ADVANTAGE - (I) is an alternative to a conventional NSAID partic. where NSAID's are contraindicated such as in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal (GI) lesions, GI bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease, or prior to surgery or while taking anticoagulants.

Dwg.0/0

ABEQ US 5691374 A UPAB: 19980112

Cyclopentenyl, di:hydrofuranyl or di:hydrothienyl benzene acid derivs. of formula (I) and their salts are new. Y = CR11R12, O or S; R1 = SO2Me, SO2NH2, SO2NHCOCF3, SONHNH2, S(O)(NH)NHCOCF3, SO2NHMe, P(O)MeNH2, P(O)Me2 or CSNH2; R2 = alkyl, cycloalkyl, 2-10C alkenyl, 2-10C alkynyl, 3-10C cycloalkenyl (opt. substd. by 1-4 of halo, 1-6C alkoxy, CN, 1-6C alkylthio, CF3, alkyl (opt. substd. by CO2R5), N3, CO2H, alkoxycarbonyl, CR5R6ORa, benzyloxy, or alkoxy (substd. by CO2R5 or NR5R6)), phenyl or naphthyl (both opt. substd. by 1-3 of halo, alkoxy (opt. substd. by CO2R5 or NR5R6), fluoroalkoxy, alkylthio, CN, CF3, alkyl, N3, CO2H, alkoxycarbonyl, CR5R6ORa, 1-6C alkyl substd. by CO2R5, or benzyloxy), Het, 5-7 membered heterocycloalkyl (contg. 1-2 of O, S or N and opt. contg. CO or sulphonyl) or benzo 5-7C carbocycle (opt. contg. a CO gp. and opt. substd. by 1-2 R'); Ra = H or 1-4C alkyl; Het = 5-membered monocyclic heteroaryl contg. 1 S, O or N and opt. 1-3 additional N, or a 6 membered monocyclic heteroaryl contg. 1-4N, or a benzo-5-7 membered heterocycle (contg. 1-2 of O, S or N and opt. CO or sulphonyl), all opt. substd. by R'; R' = halo, alkyl, alkoxy, alkylthio, CN, CF3, N3, CR5R6OR''; R'' = H or alkyl; R3, R11, R12 = phenyl, benzyl, heteroaryl, heteroarylmethyl (all opt. substd. by 1-2 R'), H, alkyl, CH2OR7, CN, CH2CN, 1-6C fluoroalkyl, F or CON(R7)2; or CR11R12 = CO or 3-7C satd. monocyclic ring; R4 = alkoxy, fluoroalkoxy, alkylthio, OH, OCOR7, SH, SCOR7, OCO2R8, SCO2R8, OCON(R7)2, SCON(R7)2, cycloalkyloxy or cycloalkylthio; R5, R6, R13, R14 = H or alkyl;

aspirin-sensitive asthmatic subjects. (I) are further useful in applications where conventional NSAIDs are contra-indicated in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis, gastrointestinal lesion or bleeding, coagulation disorders (e.g anaemia such as

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hypoprothrombinaemia), haemophilia or other bleeding problems, kidney disease and those patients taking anticoagulants and in treating patients prior to surgery. Dwg.0/0 ANSWER 91 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD 1997-020819 [02] WPIDS C1997-006665 New furyl, thienyl or cyclopentenyl benzene-sulphonamide or analogue with selective cyclooxygenase-2 inhibitory activity, useful e.g. as antiinflammatories, for viral infections, pain, etc.. BLACK, C; GRIMM, E; LEGER, S; WANG, Z (MERI) MERCK FROSST CANADA INC CYC 70 A1 19961121 (199702) * EN 110p RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD W: AL AM AU AZ BB BG BR BY CA CN CZ EE GE HU IS JP KG KR KZ LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA US UZ VN AU 9656424 A 19961129 (199712) A 19971125 (199802) US 5691374 24p EP 828724 A1 19980318 (199815) EN R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE JP 11505534 W 19990521 (199931) 124p AU 707773 B 19990722 (199940) B1 20011205 (200203) EN EP 828724 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE DE 69617676 E 20020117 (200213) WO 9636623 A1 WO 1996-CA306 19960515; AU 9656424 A AU 1996-56424 19960515; US 5691374 A US 1995-443620 19950518; EP 828724 A1 EP 1996-913412 19960515, WO 1996-CA306 19960515; JP 11505534 W JP 1996-534418 19960515, WO 1996-CA306 19960515; AU 707773 B AU 1996-56424 19960515; EP 828724 B1 EP 1996-913412 19960515, WO 1996-CA306 19960515; DE 69617676 E DE 1996-617676 19960515, EP 1996-913412 19960515, WO 1996-CA306 19960515 FDT AU 9656424 A Based on WO 9636623; EP 828724 A1 Based on WO 9636623; JP 11505534 W Based on WO 9636623; AU 707773 B Previous Publ. AU 9656424, Based on WO 9636623; EP 828724 B1 Based on WO 9636623; DE 69617676 E Based on EP 828724, Based on WO 9636623 19950518 PRAI US 1995-443620 1997-020819 [02] WPIDS 9636623 A UPAB: 19970108 Cyclopentenyl, di:hydrofuranyl or di:hydrothienyl benzene acid derivs. of formula (I) and their salts are new. Y = CR11R12, O or S; R1 = SO2Me, SO2NH2, SO2NHCOCF3, SONHNH2, S(O)(NH)NHCOCF3, SO2NHMe, P(O)MeNH2, P(O)Me2 or CSNH2; R2 = alkyl, cycloalkyl, 2-10C alkenyl, 2-10C alkynyl, 3-10C cycloalkenyl (opt. substd. by 1-4 of halo, 1-6C alkoxy, CN, 1-6C alkylthio, CF3, alkyl (opt. substd. by CO2R5), N3, CO2H, alkoxycarbonyl, CR5R6ORa, benzyloxy, or alkoxy (substd. by CO2R5 or NR5R6)), phenyl or naphthyl (both opt. substd. by 1-3 of halo, alkoxy (opt. substd. by CO2R5 or NR5R6), fluoroalkoxy, alkylthio, CN, CF3, alkyl, N3, CO2H, alkoxycarbonyl, CR5R6ORa, 1-6C alkyl substd. by CO2R5, or benzyloxy), Het, 5-7 membered heterocycloalkyl (contg. 1-2 of O, S or N and opt. contg. CO or sulphonyl) or benzo 5-7C carbocycle (opt. contg. a CO gp. and opt. substd. by 1-2 R'); Ra = H or 1-4C alkyl; Het = 5-membered monocyclic heteroaryl contg. 1 S, O or N and opt. 1-3 additional N, or a 6 membered monocyclic heteroaryl contg. 1-4N, or a benzo-5-7 membered heterocycle

(contg. 1-2 of O, S or N and opt. CO or sulphonyl), all opt. substd. by R'; R' = halo, alkyl, alkoxy, alkylthio, CN, CF3, N3, CR5R6OR''; R'' = H

1996-22128P 19960718, Provisional US 1996-27139P 19961001, Provisional US 1997-41814P 19970408, US 1997-893395 19970711; NO 9900191 A WO 1997-CA486 19970708, NO 1999-191 19990115; EP 912518 A1 EP 1997-929067 19970708, WO 1997-CA486 19970708; CZ 9900130 A3 WO 1997-CA486 19970708, CZ 1999-130 19970708; CN 1225085 A CN 1997-196377 19970708; BR 9710372 A BR 1997-10372 19970708, WO 1997-CA486 19970708; US 6001843 A Provisional US 1996-22128P 19960718, Provisional US 1996-27139P 19961001, Provisional US 1997-41814P 19970408, Div ex US 1997-893395 19970711, US 1998-181887 19981029; JP 11514008 W WO 1997-CA486 19970708, JP 1998-506397 19970708; SK 9900036 A3 WO 1997-CA486 19970708, SK 1999-36 19970708; HU 9903974 A2 WO 1997-CA486 19970708, HU 1999-3974 19970708; US 6071936 A Provisional US 1996-22128P 19960718, Provisional US 1996-27139P 19961001, Provisional US 1997-41814P 19970408, Div ex US 1997-893395 19970711, Div ex US 1998-181887 19981029, US 1999-312790 19990517; AU 723179 B AU 1997-33319 19970708; NZ 333230 A NZ 1997-333230 19970708, WO 1997-CA486 19970708; MX 9900668 A1 MX 1999-668 19990115; KR 2000067891 A WO 1997-CA486 19970708, KR 1999-700340 19990118; JP 3251945 B2 WO 1997-CA486 19970708, JP 1998-506397 19970708 FDT AU 9733319 A Based on WO 9803484; EP 912518 A1 Based on WO 9803484; CZ 9900130 A3 Based on WO 9803484; BR 9710372 A Based on WO 9803484; US 6001843 A Div ex US 5861419; JP 11514008 W Based on WO 9803484; HU 9903974 A2 Based on WO 9803484; US 6071936 A Div ex US 5861419, Div ex US 6001843; AU 723179 B Previous Publ. AU 9733319, Based on WO 9803484; NZ 333230 A Based on WO 9803484; KR 2000067891 A Based on WO 9803484; JP 3251945 B2 Previous Publ. JP 11514008, Based on WO 9803484

PRAI GB 1997-9291 19970507; US 1996-22128P 19960718; GB 1996-16126 19960801; US 1996-27139P 19961001; GB 1996-21420 19961015; US 1997-41814P 19970408; US 1997-893395 19970711; US 1998-181887 19981029; US 1999-312790 19990517

AN 1998-159099 [14] WPIDS

AB WO 9803484 A UPAB: 19980406

Substituted 3-phenylpyridines of formula (I) and their salts are new. R1 = CH3, NH2, NHC(0)CF3 or NHCH3; Ar = phenyl or pyridinyl (or the N-oxide), (both mono-, di- or trisubstituted by H, halo, 1-6C alkoxy, 1-6C alkylthio, CN, 1-6C alkyl, 1-6C fluoroalkyl, N3, -CO2R3, OH, -C(R4)(R5)-OH, -(1-6C alkyl)CO2R6 or 1-6C fluoroalkoxy); R2 = halo, 1-6C alkoxy, 1-6C alkylthio, CN, 1-6C alkyl, 1-6C fluoroalkyl, N3, -CO2R7, OH, -C(R8)(R9)-OH, -(1-6C alkyl)-CO2R10, 1-6C fluoroalkoxy, NO2, NR11R12 or NHCOR13; R3-R13 = H or 1-6C alkyl; or R4+R5, R8+R9 or R11+R12 complete a saturated monocyclic ring of 3-7 atoms.

USE - (I) are used to treat cyclooxygenase mediated diseases since they are selective inhibitors of cyclooxygenase-2 (COX-2) as opposed to cyclooxygenase-1 (COX-1). (I) are used to treat inflammatory diseases susceptible to treatment with a NSAID (all claimed). (I) are used to treat pain, fever and inflammation (e.g. rheumatic fever, influenza and other viral infection symptoms, common cold, lower back and neck pain, dysmenorrhea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, rheumatoid arthritis, degenerative joint diseases, osteoarthritis, gout and ankylosing spondylitis, bursitis, burns and injuries following surgery and dental procedures). (I) may inhibit cellular neoplastic transformations and metastatic tumour growth and can be used to treat cancer and cyclooxygenase-mediated proliferative disorders which occur in diabetic retinopathy and tumour angiogenesis. (I) also inhibit prostanoid-induced smooth muscle contraction by preventing the synthesis of contractile prostanoids and are used to treat dysmenorrhea, premature labour, asthma and eosinophil-related disorders. (I) are also used to treat Alzheimer's disease, to decrease bone loss, particularly in postmenopausal women (e.g. in treatment of osteoporosis) and to treat (I) are administered e.g. orally in a daily dosage of 0.01-140 glaucoma. (preferably 0.5-7) mg/kg.

ADVANTAGE - Because of their high inhibitory activity and specificity, side effects associated with inhibition of COX-1 are avoided e.g. gastrointestinal toxicity, reduced renal side effects, reduced effect on bleeding times and lessened ability to induce asthma attacks in

An angiogenesis inhibiting composition comprises: (A) an angiogenesis inhibiting compound; and (B) an antiinflammatory drug specifically a steroid or a non-steroidal antiinflammatory drug (NSAID).

Also claimed is a method for inhibiting angiogenesis or treating an angiogenesis-dependent disease in a human or animal, involving administration of a composition containing an NSAID and optionally (A) or (for treatment of angiogenesis-dependent diseases) a composition containing (A) and (B) as above.

USE - The angiogenesis-dependent diseases to be treated are specifically macular degeneration, diabetic retinopathy, neovascular glaucoma, retrolental fibroplasia, proliferative vitreo-retinopathy, solid or blood-bourne tumours, leukaemia, haemangioma, psoriasis, Kaposi's sarcoma, Crohn's disease, ulcerative colitis, cancer, retinopathy or prematurity, corneal graft rejection, epidemic keratoconjunctivitis, vitamin A deficiency, contact lens over-wear, atopic or superior limbic keratitis.

ADVANTAGE - The combination of (A) and (B) is effective in inhibiting angiogenesis even on oral administration, providing a simplified treatment (e.g. by self-administration), whereas (A) alone are only effective topically or by injection. NSAID's have been found to be angiogenesis inhibitors even in the absence of (A), and have an additive effect in combination with (A).

Dwg.0/8

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ANSWER 90 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
L19
AN
     1998-159099 [14]
                       WPIDS
DNC
    C1998-051254
     New substituted 3-phenylpyridines are selective cyclooxygenase-2
TI
     inhibitors - used to treat inflammatory diseases e.g. rheumatic fever,
     pain, cancer, diabetic retinopathy, tumour angiogenesis, asthma,
     Alzheimer's disease and osteoporosis.
DC
IN
     DUBE, D; FORTIN, R; FRIESEN, R; GAUTHIER, J Y; WANG, Z
PA
     (MERI) MERCK FROSST CANADA INC; (MERI) MERCK FROSST CANADA & CO; (MERI)
     MERCK & CO INC
CYC
    79
PΙ
     WO 9803484
                   A1 19980129 (199814)* EN
                                              q88
        RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT
            SD SE SZ UG ZW
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W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE HU IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AU 9733319 A 19980210 (199827)

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A 19980527 (199827)
ZA 9706335
                                       85p
            A 19990119 (199911)
US 5861419
NO 9900191
             A 19990316 (199921)
EP 912518
            A1 19990506 (199922) EN
   R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI
CZ 9900130 A3 19990616 (199929)
CN 1225085
            A 19990804 (199949)
BR 9710372 A 19990817 (199954)
US 6001843
            A 19991214 (200005)
JP 11514008 W 19991130 (200007)
                                      115p
SK 9900036 A3 19991210 (200008)
HU 9903974
            A2 20000328 (200025)
US 6071936 A 20000606 (200033)
AU 723179
            B 20000817 (200044)
            A 20000825 (200049)
NZ 333230
MX 9900668
            A1 19990401 (200055)
KR 2000067891 A 20001125 (200130)
            B2 20020128 (200214)
JP 3251945
                                       28p
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ADT WO 9803484 A1 WO 1997-CA486 19970708; AU 9733319 A AU 1997-33319 19970708; ZA 9706335 A ZA 1997-6335 19970717; US 5861419 A Provisional US

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PRAI WO 1996-IB1395
                      19961209
                       WPIDS
     1998-299932 [27]
          846689 A UPAB: 19980709
AB
     Benzimidazole derivatives of formula (I) and their salts are new: Ar = Ph,
     3-8C cycloalkyl, 4-8C cycloalkenyl or Het (bonded to Y through C); Het =
     e.g. pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrrolyl, furyl,
     thienyl, oxazolyl, thiazolyl, isooxazolyl, isothiazolyl or imidazolyl; X1
     = e.g. H, halo, 1-4C alkyl (optionally substituted), OH, 1-4C alkoxy, 1-4C
     alkoxy(1-4C)alkyl, NH2, 1-4C alkylamino, di(1-4C)alkylamino,
     amino(1-4C)alkyl, 1-4C alkylamino(1-4C)alkyl, di(1-4C)alkylamino(1-
     4C) alkyl, 1-4C alkanoylamino, di(1-4C) alkanoylamino, 1-4C alkyl(1
     4C) alkanoylamino, 1-4C alkylsulphonylamino, 1-4C alkanoyl, carboxyl, 1-4C
     alkoxycarbonyl, aminocarbonyl, 1-4C alkylaminocarbonyl,
     di(1-4C)alkylaminocarbonyl, CN or NO2; X2, X3 = 1-4C alkyl (optionally
     substituted) halo, OH, 1-4C alkoxy, mercapto, 1-4C alkylthio, 1-4C
     alkylsulphinyl, 1-4C alkylsulphonyl, 1-4C alkanoyl, carboxyl, 1-4C
     alkoxycarbonyl, aminocarbonyl, 1-4C alkylaminocarbonyl,
     di(1-4C)alkylaminocarbonyl, CN, NO2, NH2, 1-4C alkylamino,
     di(1-4C)alkylamino or 1-4C alkylsulphonylamino; Y = CR1=CR2 or C=C; R1, R2
     = H, Me, Et or halo; l = 0-4; and m, n = 0-3; with provisos.
          USE - (I) are used for treating conditions in which prostaglandins
     are implicated as pathogens (claimed). They are cyclooxygenase (COX)
     inhibitors which inhibit the biosynthesis of prostaglandins by intervening
     with the action of COX on arachidonic acid to treat inflammation and
     related disorders. They are selective for COX-2 over COX-1 and may be used
     to inhibit cellular neoplastic transformations and metastic tumour growth
     in the treatment of cancer. They can also be used to treat and prevent
     diabetic retinopathy, tumour angiogenesis, dysmenorrhea,
     premature labour, asthma, eosinophil related disorders, Alzheimer's
     disease or bone loss (e.g. osteoarthritis).
          ADVANTAGE - They can be used as an alternative to NSAIDS
     especially where NSAIDS are contraindicated e.g. patients with
     peptic ulcers, gastritis, regional enterotis, ulcerative
     colitis, diverticulitis or recurrent history of gastrointestinal
     legions or bleeding, coagulation disorders, kidney disease and prior to
     surgery of taking anticoagulants.
     Dwg.0/0
L19
    ANSWER 89 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN
     1998-286556 [25]
                        WPIDS
DNC
    C1998-088702
     Orally effective angiogenesis inhibiting combination -
TΙ
     containing angiogenesis inhibitor, e.g. thalidomide, and
     antiinflammatory, e.g. sulindac, useful in tumour treatment.
DC
IN
     DAMATO, R J; D'AMATO, R J
PΑ
     (CHIL-N) CHILDRENS MEDICAL CENT
CYC
PΙ
                  A2 19980514 (199825) * EN
                                              63p
        RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT
            SD SE SZ UG ZW
         W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
            GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN
            MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN
            YU ZW
    AU 9851973
                   A 19980529 (199841)
                   A2 19991215 (200003)
                                        EN
        R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
    WO 9819649 A2 WO 1997-US20116 19971104; AU 9851973 A AU 1998-51973
ADT
     19971104; EP 963200 A2 EP 1997-946884 19971104, WO 1997-US20116 19971104
    AU 9851973 A Based on WO 9819649; EP 963200 A2 Based on WO 9819649
FDT
PRAI US 1997-963058
                      19971103; US 1996-28708P
                                                 19961105
AN
    1998-286556 [25]
                       WPIDS
AB
         9819649 A UPAB: 19980624
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1998-458786 [40]
                       WPIDS
AN
     1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33];
CR
     1996-221734 [22]; 1997-245037 [22]; 1997-280687 [25]; 1997-435662 [41];
     1998-521151 [44]
           863134 A UPAB: 20020213
AB
     2-(3,5-Difluorophenyl)-3-(4-(methylsulphonyl)phenyl)-2-cyclopenten-1-one
     of formula (I) is new. Also claimed is crystalline (I).
          USE - (I) is a cyclooxygenase-2 (COX-1) inhibitor used to treat
     non-chronic headache, pain or swelling, osteoarthritis, rheumatoid
     arthritis and inflammatory diseases susceptible to treatment with a
     non-steroidal antiinflammatory drug (NSAID) (all claimed).
     is useful for treating pain, fever and inflammation in a variety of
     conditions e.g. rheumatic fever, symptoms associated with influenza or
     other viral infections, common cold, lower back and neck pain,
     dysmenorrhoea, headache, toothache, sprains and strains, myositis,
     neuralgia, synovitis, arthritis (including rheumatoid arthritis),
     degenerative joint diseases (including osteoarthritis), gout and
     ankylosing spondylitis, bursitis, burns and injuries following surgical
     and dental procedures. (I) inhibits cellular neoplastic transformations
     and metastatic tumour growth and can be used in the treatment of cancer
     (e.g. cancer of the colon). (I) is also used to treat and/or prevent
     COX-mediated proliferative disorders such as may occur in diabetic
     retinopathy and tumour angiogenesis. (I) inhibits
     prostanoid-induced smooth muscle contraction by preventing the synthesis
     of contractile prostanoids and may be of use in the treatment of
     dysmenorrhoea, premature labour, asthma and eosinophil related disorders
     and is also useful in treating Alzheimer's disease, for decreasing bone
     loss, particularly in postmenopausal women and for treatment of glaucoma.
     (I) is useful as an alternative to prior art NSAIDs,
     particularly where they are contra-indicated in patients with peptic
     ulcers, gastritis, regional enteritis, ulcerative
     colitis, diverticulitis or with a recurrent history of
     gastrointestinal lesions, gastrointestinal bleeding, coagulation disorders
     including anaemia such as hypopropthrombinaemia, haemophilia or other
     bleeding problems, kidney disease and those prior to surgery or taking
     anticoagulants. (I) is administered in a dosage of 10-250 mg once or
     twice a day.
          ADVANTAGE - (I) is specific for COX-2 rather than COX-1 and has fewer
     side effects than prior art NSAIDs, particularly
     gastrointestinal toxicity, renal side effects, reduced effects on bleeding
     times and lower ability to induce asthma attacks in aspirin-sensitive
     asthmatic patients.
     Dwg.0/0
L19 ANSWER 88 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
     1998-299932 [27]
AN
                       WPIDS
DNC C1998-093557
ТT
     New benzimidazole derivatives are cyclo-oxygenase inhibitors - used for
     treating conditions in which prostaglandins are implicated as pathogens,
     cancer, diabetic retinopathy and tumour angiogenesis.
DC
     MANO, T; OKUMURA, Y; STEVENS, R W
IN
     (PFIZ) PFIZER INC; (PFIZ) PFIZER SEIYAKU KK
PA
CYC 28
PΤ
                  A1 19980610 (199827)* EN
    EP 846689
                                              26p
         R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO
            SE SI
     JP 10168066 A 19980623 (199835)
                                              23p
                 A 19980609 (199839)
     CA 2223551
                 A 19990518 (199925)
     BR 9706241
     MX 9710034
                 A1 19980601 (200009)
ADT EP 846689 A1 EP 1997-309761 19971203; JP 10168066 A JP 1997-350154
     19971205; CA 2223551 A CA 1997-2223551 19971204; BR 9706241 A BR 1997-6241
     19971209; MX 9710034 A1 MX 1997-10034 19971209
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Provisional US 1997-40794P 19970314, US 1998-42168 19980313; JP 2001514668 W JP 1998-539978 19980312, WO 1998-CA225 19980312; AU 741981 B Div ex AU 1996-71236 19961009, Div ex AU 1996-72736 19961029, AU 1998-67142 19980312 FDT AU 9867142 A Based on WO 9841516; EP 970067 A1 Based on WO 9841516; JP 2001514668 W Based on WO 9841516; AU 741981 B Div ex AU 703871, Div ex AU 711902, Previous Publ. AU 9867142, Based on WO 9841516 PRAI GB 1997-7488 19970414; US 1997-40794P 19970314; US 1998-42168 19980313 ΑN 1998-521151 [44] WPIDS 1995-051970 [07]; 1995-255022 [33]; 1996-221734 [22]; 1997-245037 [22]; CR 1997-280687 [25]; 1997-435662 [41]; 1998-458786 [40] 9841516 A UPAB: 20020213 AB Methyl sulphonyl)phenyl-2-(5H)-furanone derivatives of formula (I) are new: R = 1-12C alkyl substituted by 1-3 Q, or 2-10C alkenyl 2-10C alkynyl, 3-12C cycloalkenyl or 5-12C cycloalkynyl (all optionally substituted by 1-3 Q); Q = F, Cl, Br, I, OH, CF3, 3-6C cycloalkyl, O, dioxolane or CN; R1 = Me, NH2, NHCOCF3 or NHMe; R2, R3 = H or 1-10C alkyl; or CR2R3 = 3-7C saturated monocyclic ring. USE - (I) are cyclooxygenase inhibitors which selectively inhibit COX-2 over COX-1 and are useful for treatment of disorders susceptible to treatment with COX-2 inhibitors and/or NSAIDs, eg rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns, injuries, following surgical and dental procedures. In addition the compounds inhibit cellular neoplastic transformations and metastatic tumour growth and can be used in the treatment of cancer. They may also be used to treat and/or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour angiogenesis. (I) also inhibit prostanoid-induced smooth muscle contraction by preventing synthesis of contractile prostanoid s and are useful in the treatment of dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are also useful in the treatment of Alzheimer's disease and for prevention of bone loss (treatment of osteoporosis) and treatment of glaucoma. By virtue of their high selectivity for COX-2 over COX-1, (I) are useful as alternatives to conventional NSAIDs, particularly where NSAIDs are contraindicated eg in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal lesions, GI bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease and those prior to surgery or taking anticoagulants. (I) can be coadministered with other active agents. Dwg.0/0 L19 ANSWER 87 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD 1998-458786 [40] ΑN WPIDS 1994-217755 [26]; 1995-051970 [07]; 1995-172512 [23]; 1995-255022 [33]; CR 1996-221734 [22]; 1997-245037 [22]; 1997-280687 [25]; 1997-435662 [41]; 1998-521151 [44] DNN N1998-358262 DNC C1998-138690 TINew 2-(3,5-di fluoro-phenyl)-3-(4-(methylsulphonyl)phenyl)-2-cyclopenten-1one inhibits cyclooxygenase-2 - used to treat non-chronic headache, pain or swelling, osteoarthritis and rheumatoid arthritis. DC B05 IN BLACK, C PA (MERI) MERCK FROSST CANADA INC CYC 22 PΙ A1 19980909 (199840)* EN 23p EP 863134 R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV NL PT RO SE SI ADT EP 863134 A1 EP 1997-302918 19970429 PRAI GB 1997-7643 19970415; US 1997-40049P 19970307

of S, O and N and optionally 1-3 additional N atoms or a 6 membered ring containing 1N and optionally 1-3 additional N atoms (both optionally substituted by halo, 1-10C alkoxy, 1-10C alkylthio, CN, 1-6C fluoroalkyl, 1-10C alkyl or N3); R4 = H, halo or 1-6C alkyl and R5 = H or 1-6C alkyl. 36 Compounds (I) are specifically claimed e.g. 5-(4-methylsulphonyl)phenyl-2-phenyl-4-phenyl-2H-pyridazin-3-one. USE - (I) are cyclooxygenase inhibitors which selectively inhibit COX-2 over COX-1 and are useful for treatment of disorders susceptible to treatment with COX-2 inhibitors and/or non steroidal antiinflammatory drugs (NSAIDs), particularly pain, fever and inflammation of conditions including rheumatic fever, symptoms associated with influenza or other viral infections, common cold, low back and neck pain, dysmenorrhoea, headache, toothache, sprains and strains, myositis, neuralgia, synovitis, arthritis, including rheumatoid arthritis, degenerative joint diseases (osteoarthritis), gout and ankylosing spondylitis, bursitis, burns, injuries, following surgical and dental procedures. (I) also inhibit cellular neoplastic transformations and metastatic tumour growth and can be used in the treatment of cancer. (I) are also used to treat and/or prevent COX-mediated proliferative disorders such as may occur in diabetic retinopathy and tumour angiogenesis . (I) also inhibit prostanoid-induced smooth muscle contraction by preventing synthesis of contractile prostanoids and are useful in the treatment of dysmenorrhoea, premature labour, asthma and eosinophil related disorders. (I) are also useful in the treatment of Alzheimer's disease and for prevention of bone loss (treatment of osteoporosis) and treatment of glaucoma. (I) are useful as alternatives to conventional NSAIDs, particularly where NSAIDs are contraindicated e.g. in patients with peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis or with a recurrent history of gastrointestinal lesions, gastrointestinal bleeding, coagulation disorders including anaemia such as hypoprothrombinaemia, haemophilia or other bleeding problems, kidney disease and those prior to surgery or taking anticoagulants. (I) can be coadministered with other active agents. The dosage of (I) is 0.01-140 mg/kg/day orally, topically, parenterally, by inhalation spray or rectally. The dosage for treating inflammation is 0.01-50 mg/kg/day. Dwg.0/0 ANSWER 86 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD 1998-521151 [44] WPIDS 1995-051970 [07]; 1995-255022 [33]; 1996-221734 [22]; 1997-245037 [22]; 1997-280687 [25]; 1997-435662 [41]; 1998-458786 [40] C1998-156556 New (methylsulphonyl)phenyl-2-(5H)-furanone derivatives - are selective cyclooxygenase 2 inhibitors, useful as antiinflammatory, antipyretic and analgesic agents. GRIMM, E; LEBLANC, Y; LEGER, S; ROY, P; WANG, Z (MERI) MERCK FROSST CANADA & CO; (MERI) MERCK FROSST CANADA INC CYC WO 9841516 A1 19980924 (199844) * EN 69p RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AU 9867142 A 19981012 (199907) A1 20000112 (200008) EP 970067 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE US 6071954 A 20000606 (200033) JP 2001514668 W 20010911 (200167) 72p B 20011213 (200210) AU 741981

ADT WO 9841516 A1 WO 1998-CA225 19980312; AU 9867142 A AU 1998-67142 19980312; EP 970067 A1 EP 1998-912164 19980312, WO 1998-CA225 19980312; US 6071954 A

L19

 $\mathbf{A}\mathbf{N}$

CR

ΤI

DC IN

PA

PΙ

DNC

DTUtility APPLICATION FS LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850 Number of Claims: 22 Exemplary Claim: 1 DRWN No Drawings LN.CNT 11257 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention relates to novel human RIP polypeptides and isolated nucleic acids containing the coding regions of the genes encoding such polypeptides. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human RIP polypeptides. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human RIP polypeptides. => s l19 85-91 bib, abs MISSING OPERATOR L19 85-91 The search profile that was entered contains terms or nested terms that are not separated by a logical operator. => d 119 85-91 bib, abs L19 ANSWER 85 OF 91 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD AN 1998-531549 [45] WPIDS DNC C1998-159416 New 5-(4-sulphonyl-phenyl)-pyridazinone derivatives - are selective cyclo-oxygenase 2 inhibitors used for treating inflammatory disease, Alzheimer's disease and glaucoma. DC IN GAUTHIER, J Y; LAU, C K; LI, C S; PRASIT, P; THERIEN, M (MERI) MERCK FROSST CANADA & CO; (MERI) MERCK FROSST CANADA INC PA CYC WO 9841511 A1 19980924 (199845)* EN PΤ 87p RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GW HU ID IL IS JP KG KR KZ LC LK LR LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK SL TJ TM TR TT UA US UZ VN YU AU 9864913 A 19981012 (199907) US 6004960 A 19991221 (200006) A1 20000202 (200011) EP 975604 EN R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE JP 2001514669 W 20010911 (200167) AU 738727 B 20010927 (200170) WO 9841511 A1 WO 1998-CA233 19980312; AU 9864913 A AU 1998-64913 19980312; ADT US 6004960 A Provisional US 1997-40791P 19970314, US 1998-42174 19980313; EP 975604 A1 EP 1998-910544 19980312, WO 1998-CA233 19980312; JP 2001514669 W JP 1998-539982 19980312, WO 1998-CA233 19980312; AU 738727 B AU 1998-64913 19980312 FDT AU 9864913 A Based on WO 9841511; EP 975604 A1 Based on WO 9841511; JP 2001514669 W Based on WO 9841511; AU 738727 B Previous Publ. AU 9864913, Based on WO 9841511 PRAI GB 1997-7487 19970414; US 1997-40791P 19970314; US 1998-42174 19980313 1998-531549 [45] WPIDS ΔN AB 9841511 A UPAB: 19981111 Pyridazinone derivatives of formula (I) are new: X = a bond, (CH2)m, CO, O, S or NR5; m = 1-2; R1 = Me, NH2 or NHCOCF3; R2 = (CR6R7) nR8; n = 0-2; R6, R7 = H, 1-10C alkyl or 1-10C fluoroalkyl; R3, R8 = 1-10C alkyl, Ph or naphthyl (both optionally substituted by 1-3 of halo 1-10C alkoxy, 1-10C alkylthio, CN, 1-6C fluoroalkyl, 1-10C alkyl or N3) or heteroaryl comprising a monocyclic 5 membered aromatic ring optionally containing one

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WO 9819649
                       Α3
                            19980625
         W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,
             EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN,
             YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
                                           AU 1998-51973
                       A1
                            19980529
                                                             19971104
     AU 9851973
                       A2
                            19991215
                                           EP 1997-946884
                                                            19971104
     EP 963200
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
         R:
             IE, FI
PRAI US 1996-28708
                            19961105
                            19971103
     US 1997-963058
                            19971104
     WO 1997-US20116
     MARPAT 129:12742
     A group of compds. that effectively inhibit angiogenesis is
AB
     provided. More specifically, thalidomide and various related compds.,e.g.
     thalidomide precursors, analogs, metabolites and hydrolysis products, have
     been shown to inhibit angiogenesis and to treat disease states
     resulting from angiogenesis. Addnl., antiinflammatory drugs,
     such as steroids and NSAIDs can inhibit angiogenesis
     -dependent diseases either alone or in combination with thalidomide and
     related compds. Importantly, these compds. can be administered orally.
L20
    ANSWER 2 OF 3 USPATFULL
AN
       2002:22462 USPATFULL
       COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING INFLAMMATORY
TT
       DISEASES
       HUNTER, WILLIAM L., VANCOUVER, CANADA
TN
PΤ
       US 2002013298
                         A1
                               20020131
       US 1999-368463
ДΤ
                          Α1
                               19990804 (9)
       Division of Ser. No. US 1998-88546, filed on 1 Jun 1998, PENDING
RLI
       Continuation-in-part of Ser. No. US 1997-980549, filed on 1 Dec 1997,
       PENDING
PRAI
       US 1996-32215
                           19961202 (60)
       US 1997-63087
                           19971024 (60)
DT
       Utility
       APPLICATION
FS
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300,
LREP
       SEATTLE, WA, 98104-7092
       Number of Claims: 45
CLMN
ECL
       Exemplary Claim: 1
DRWN
       110 Drawing Page(s)
LN.CNT 8318
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods and compositions for treating or preventing inflammatory
AB
       diseases such as psoriasis or multiple sclerosis are provided,
       comprising the step of delivering to the site of inflammation an
       anti-microtubule agent, or analogue or derivative thereof.
L20
    ANSWER 3 OF 3 USPATFULL
       2002:8489 USPATFULL
AN
TI
       Retinoid receptor interacting polynucleotides, polypeptides, and
       antibodies
TN
       Shi, Yanggu, Gaithersburg, MD, UNITED STATES
       Ruben, Steven M., Olney, MD, UNITED STATES
PΙ
       US 2002004489
                          Α1
                               20020110
ΑI
       US 2001-788600
                          A1
                               20010221 (9)
RLI
       Continuation-in-part of Ser. No. WO 2000-US22351, filed on 15 Aug 2000,
       UNKNOWN
PRAI
       US 1999-148757
                           19990816 (60)
       US 2000-189026
                           20000314 (60)
```

```
=> s lupus
      101544 LUPUS
=> s 11 and 14
         3109 L1 AND L4
=> s l1 and l5
         586 L1 AND L5
L10
=> s l1 and l7
        7531 L1 AND L7
=> s l1 and l8
L12
         751 L1 AND L8
=> s angiogenesis
       61491 ANGIOGENESIS
L13
=> s neovascular generat####
 5 FILES SEARCHED...
            0 NEOVASCULAR GENERAT####
=> s neovasculargenerat####
            0 NEOVASCULARGENERAT####
=> s 113 and 13
         716 L13 AND L3
=> s 14 and 116
         305 L4 AND L16
L17
=> s 113 and 15
         619 L13 AND L5
=> s 116 and 15
        91 L16 AND L5
L19
=> s 116 and 16
         3 L16 AND L6
=> s 116 and 17
         281 L16 AND L7
L21
=> s 116 and 18
          60 L16 AND L8
L22
=> d 120 1-3 bib, ab
L20 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN
    1998:341491 CAPLUS
DN
    129:12742
ΤI
    Methods and compositions using thalidomide or other angiogenesis
    -inhibitory compound and anti-inflammatory agent for inhibition of
    angiogenesis
IN
    D'Amato, Robert J.
PA
    Children's Medical Center, USA
    PCT Int. Appl., 63 pp.
SO
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 1
    PATENT NO.
                   KIND DATE
                                        APPLICATION NO. DATE
    -----
                                         -----
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PI

WO 9819649

A2

19980514

WO 1997-US20116 19971104

accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE): file caplus, uspatfull, wpids, toxlit, toxlin, drugu, medline, biosis

'FILE' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE): file caplus, uspatfull, wpids, toxlit, drugu, medline, biosis

'FILE' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE):end

=> file caplus, uspatfull, wpids, toxlit, drugu, medline, biosis
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
0.30
0.30

FILE 'CAPLUS' ENTERED AT 16:11:11 ON 13 MAR 2002 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'USPATFULL' ENTERED AT 16:11:11 ON 13 MAR 2002 CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 16:11:11 ON 13 MAR 2002 COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE 'TOXLIT' ENTERED AT 16:11:11 ON 13 MAR 2002

FILE 'DRUGU' ENTERED AT 16:11:11 ON 13 MAR 2002 COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE 'MEDLINE' ENTERED AT 16:11:11 ON 13 MAR 2002

FILE 'BIOSIS' ENTERED AT 16:11:11 ON 13 MAR 2002 COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s NSAID or NSAID##

L1 32162 NSAID OR NSAID##

=> s nonsteroidal(4a)antiinflammator######

L2 14637 NONSTEROIDAL(4A) ANTIINFLAMMATOR######

=> s 11 or 12

L3 41818 L1 OR L2

=> s cancer##

L4 1156548 CANCER##

=> s ulcerative colitis

L5 39399 ULCERATIVE COLITIS

=> s syphilis

L6 26917 SYPHILIS

=> s arthritis

L7 243552 ARTHRITIS

APPLICATION DETAILS:

PATENT NO KIND	AP	PLICATION	DATE			
\	t of US	1990-601644 1993-16179 1993-162388 1994-318160	19901023 19930211 19931207 19941005			

PRIORITY APPLN. INFO: US 1994-318160 19941005; US 1990-601644

19901023; US 1993-16179

1993-162388 19931207

ΑB 5681964 A UPAB: 19980126

> A polyethylene glycol ester prodrug comprises a steroidal, antiviral, immunomodulating, anti-tumour, neovascular or nonsteroidal compound. The non-steroidal compound is indomethacin, didooxyinosine (DDI) and gancyclovir and the compound is linked via an ester linkage to a polyethylene glycol of formula HO(CH2CH2)nH where n = 2-12.

USE - The prodrugs are used to treat disease conditions or symptoms e.g. they can be used as anti-inflammatories, antivirals, immunomodulators, anti-tumour agents, to inhibit e.g. neovascularisation.

ADVANTAGE - The prodrug in the case of flurbiprofen is non-irritating unlike flurbiprofen itself. Dwg.0/0

L110 ANSWER 54 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER:

1996-412570 [41]

DOC. NO. CPI:

C1996-129990 TITLE:

Inhibition of mammalian hair growth without side effects

- uses e.g. non steroidal suppressor

of angiogenesis, sp. useful for women with

WPIDS

hirsutism.

DERWENT CLASS:

B04 B05 D21

INVENTOR(S): PATENT ASSIGNEE(S): AHLUWALIA, G S; SHANDER, D; STYCZYNSKI, P; STYCZNSKI, P (HAND-I)/HANDELMAN J H; (AHLU-I) AHLUWALIA G S; (SHAN-I)

19930211; US

SHANDER D; (STYC-I) STYCZYNSKI P

COUNTRY COUNT:

72

PATENT INFORMATION:

PA	PENT							***	EEK]	LА		-			
WO	962																
	RW:	ΑT	BE	CH	DE	DK	EA	ES	FR	GB	GR	ΙE	IT	KE	LS	LU	ì

MC MW NL OA PT SD SE

W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN

24

AU 9653009 A 19960918 (199701)

WO 9626712 A3 19961121 (199702) ZA 9601600 A 19961129 (199702)

EP 812185 A1 19971217 (199804)

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

MX 9706522 A1 19971101 (199902)

BR 9607060 A 19981215 (199905)

JP 11501035 19990126 (199914) W 31

AU 719106 В 20000504 (200030) US 6093748 A 20000725 (200038)

APPLICATION DETAILS:

Searched by Barb O'Bryen, STIC 308-4291



/ LREP Angres, Isaac

CLMN Number of Claims: 19 ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 925

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of treatment for inflammatory and autoimmune dermatoses which comprises topical and/or systemic administration of a therapeutically-effective amount of thalidomide alone or in combination with other dermatological agents.

L16 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2002 ACS

AN 1997:593792 CAPLUS

DN 127:242709

TI Thalidomide may impede cell migration in primates by down-regulating integrin .beta.-chains: potential therapeutic utility in solid malignancies, proliferative retinopathy, inflammatory disorders, neointimal hyperplasia, and osteoporosis

AU Mccarty, M. F.

CS Nutrition 21, San Diego, CA, 92109, USA SO Med. Hypotheses (1997), 49(2), 123-131

CODEN: MEHYDY; ISSN: 0306-9877

PB Churchill Livingstone

DT Journal; General Review

LA English

A review with 108 refs. A growing no. of human inflammatory disorders are AB reported to respond to treatment with thalidomide, and recently this drug has been shown to inhibit angiogenesis in the rabbit, in doses which can elicit teratogenicity in this species. Studies in marmosets and humans indicate that thalidomide, and a teratogenic analog, decrease the expression of .beta. integrin subunits, most notably .beta.3 and the .beta.2 produced by leukocytes. Since integrins are crucial for cell-matrix interactions, and the .beta.2 integrins of leukocytes mediate adhesion to endothelium, it is reasonable to postulate that thalidomide inhibits cell migration in susceptible species, and that this accounts for its anti-inflammatory, anti-angiogenic, and teratogenic activity. This perspective suggests that thalidomide will show utility in the prevention or treatment of a wide range of disorders, including solid tumors, proliferative retinopathies, many inflammatory diseases, neointimal hyperplasia, and osteoporosis. It is likely that dietary fish oil - as well as selective inhibitors of urokinase, when and if they become clin. available - will complement the efficacy of thalidomide in most if not all of these applications.

L16 ANSWER 27 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1996:224768 BIOSIS

DN PREV199698780897

TI New uses of thalidomide.

AU Anonymous

SO Medical Letter (New Rochelle), (1996) Vol. 38, No. 968, pp. 15-16. ISSN: 0025-732X.

DT Article

LA English

AB Investigational drug status has been granted to thalidomide in the US for clinical trials in erythema nodosum leprosum, aphthous ulcers in patients with and without HIV (human immunodeficiency virus) infection, Behcet's disease, chronic graft versus host disease, inflammatory dermatoses and AIDS (acquired immune deficiency syndrome) wasting. The immunomodulator has several serious side effects, the most common being teratogenicity. The drug is available from Celgene, Andrulis, and the FDA.

L16 ANSWER 28 OF 28 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1995-31063 DRUGU P

TI Thalidomide analogs suppress rat collagen arthritis.

Oliver S J; Cheng T P; Banquerigo L; Brahn E ΑU CS Univ.California Los Angeles, Cal., USA LO Arthritis Rheum. (38, No. 6, Suppl., R10, 1995) so ISSN: 0004-3591 CODEN: ARHEAW UCLA School of Medicine, Los Angeles 90024, U.S.A. AVLA English DTJournal AB; LA; CT FΑ FS Literature

AΒ

To evaluate therapeutic potential in collagen-induced arthritis (CIA), rats were administered p.o. thalidomide or either of 2 analogs, EM-12 or supidimide. Suppression of inflammatory synovitis was lower in all experimental groups. The EM-12 analog was the most efficacious and b.i.d. thalidomide was better than once daily. Incidence of arthritis onset was comparable among all groups. Strong cell-mediated and humoral responses to type II collagen (CII) were similar in the experimental and control groups. Results suggest that thalidomide and its analogs may be effective in treating inflammatory synovitis and that these benefits might be related to modulation of TNF-alpha and/or angiogenesis. (conference abstract).